REMARKS

Claims 28-30 are pending in the present application.

In the Office Action, claims 28-30 are rejected under 35 U.S.C. 103(a) as obvious over Peskind et al., Neurology, 2001, vol. 56, pp. 1094-1098 ("Peskind"). It is alleged in the Office Action that Peskind discloses that elevated cortisol levels are associated with elevated risk of Alzheimer's disease, so that it would have been obvious to administer a medication to lower cortisol level so as to lower the risk of Alzheimer's disease.

The rejection is respectfully traversed. It is submitted that Peskind fails to recognize or exploit a relationship between cortisol level and Alzheimer's disease. For example, Peskind states that "[t]he lack of relationship between cognitive function and CSF cortisol level in the subjects with AD [Alzheimer's disease] makes it unlikely that higher CSF cortisol level reflects disease severity" (Peskind at page 1097, left col., last full paragraph). Thus, Peskind cannot suggest measuring or lowering CSF cortisol levels to diagnose or treat AD because Peskind has not identified a relationship between CSF cortisol levels and AD.

In support of the above explanation, Applicant refer to the prior publication by Peskind et al., namely, Craft et al., Insulin Metabolism in Alzhiemer's Disease Differs According to Apolipoprotein E Genotype and Gender, Neuroendocrinology 1999;70:146-152 ("Peskind 1999"), which is submitted in an Information Disclosure Statement with this paper. Peskind 1999 reports administration of intravenous insulin to Alzheimer's disease patients whose plasma insulin is already high. This procedure would be expected to lead to higher CSF cortisol. Thus, Peskind 1999 already failed to administer a medication to reduce CSF cortisol to normal. This teaching of Peskind 1999 is not contradicted in Peskind 2001. Therefore, Peskind 1999 as well as Peskind

2001 fail to teach or suggest detecting or treating Alzheimer disease in a patient with regard to CSF cortisol level.

This deficiency of Peskind 2001 is confirmed by a subsequent publication by Peskind et al., namely, Aisen et al., Steroid-induced elevation of glucose in Alzheimer's disease: relationship to gender, apolipoprotein E genotype and cognition, Psychoneuroendocrinology 28 (2003) 113-120 ("Peskind 2003"), which is also submitted in the IDS. In this 2003 publication, Peskind et al. report a study of prednisone administration in Alzheimer's disease. Prednisone is a corticosteroid which uses the same glucocorticosteroid receptors as cortisol. Therefore, administering prednisone will tend to increase the effects of cortisol in CSF. Thus, the 2003 publication makes clear that Peskind et al. 2001 would not have provided a suggestion or motivation to detect or treat Alzheimer disease in a patient with regard to CSF cortisol level, because the person of the art would have recognized that the focus of the Peskind studies is on therapeutic diagnostics and treatments that do not reduce CSF cortisol.

In contrast, in the presently claimed invention, a level of cortisol in the cerebro-spinal fluid (CSF) of the patient is measured or detected, as recited in respective present claims 28-29, so that Alzheimer's disease can be identified or treated, as further recited in respective present claims 28-29. An advantage of this feature is that early detection of Alzheimer's disease through measurement of cortisol levels can be facilitated. This feature of the presently claimed invention and its advantages are not taught or suggested in Peskind, and therefore, the present claims are not anticipated by, and not obvious over, the cited reference.

In view of the above, it is submitted that the rejection over Peskind should be withdrawn.

Next, in the Office Action, claims 28-30 are rejected under 35 U.S.C. 103(a) as obvious

over Swaab et al., Journal of Endocrinology, 1994, vol. 6, pp. 681-687 ("Swaab"). It is alleged in the Office Action that Swaab discloses increased cortisol levels in subjects with Alzheimer's disease, so that it would have been obvious to lower cortisol level so as to lower the risk of Alzheimer's disease.

This rejection is also respectfully traversed. Swaab does not establish a connection between elevated CSF-cortisol levels and diagnosing or treating Alzheimer's disease ("AD"). In particular, Swaab explains that the increased levels of CSF cortisol in "a real neurobiological phenomenon reflecting the hyperactivity of the HPA-axis in those two conditions [around the moment of death" (Swaab at page 684, right col.). Swaab also asserts that "[a]lthough CSF-cortisol levels may be a good research tool for post-mortem estimation of the responsiveness of the HPA-axis, it is unlikely that increased CSF-cortisol levels might help in the diagnosis of Alzheimer's disease" (Swaab at page 684, right col.). In other words, Swaab has focused on age groups before the onset of AD, rather than patients having AD, so that Swaab does not suggest using CSF-cortisol levels to diagnose the risk of AD, let alone administering medication to lower CSF-cortisol levels.

It is noted that the Swab publication is referenced in Peskind et al. 2001 discussed above. Peskind comments that the Swaab study related to "CSF samples obtained post mortem" (Peskind at page 1095, left col.).

In contrast, in the presently claimed invention, a level of cortisol in the cerebro-spinal fluid (CSF) of the patient is measured or detected, as recited in respective present claims 28-29, so that Alzheimer's disease can be identified or treated, as further recited in respective present claims 28-29. An advantage of this feature is that early detection of Alzheimer's disease through

measurement of cortisol levels can be facilitated. This feature of the presently claimed invention and its advantages are not taught or suggested in Swaab, and therefore, the present claims are not anticipated by, and not obvious over, the cited reference.

In view of the above, it is submitted that the art rejection should be withdrawn.

In the event there is, in the Examiner's opinion, any outstanding issue and such issue may be resolved by means of a telephone interview, the Examiner is respectfully requested to contact the undersigned attorney at the telephone number listed below.

In the event this paper is not considered to be timely filed, the Applicants hereby petition for an appropriate extension of the response period. Please charge the fee for such extension and any other fees which may be required to our Deposit Account No. 50-2866.

Respectfully submitted,

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